

00150617 001106

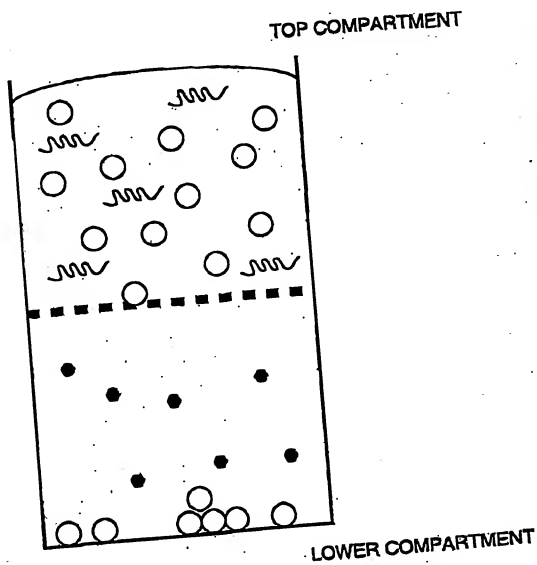


FIGURE 1

Effect of Peptide 3 with MCP-1 (50ng/ml)

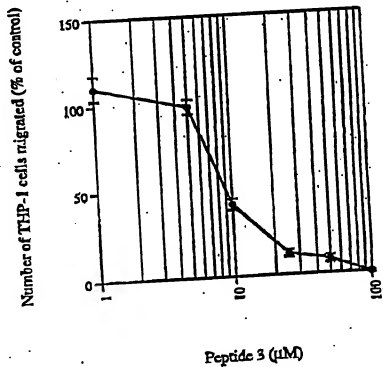


FIGURE 2

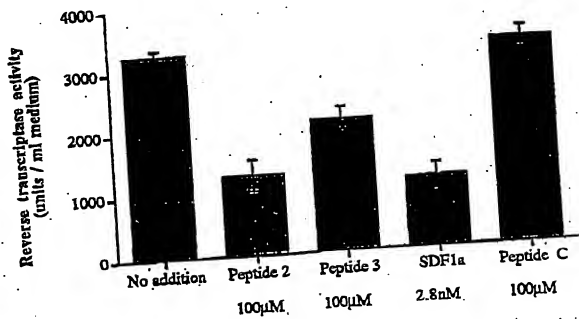


FIGURE 3

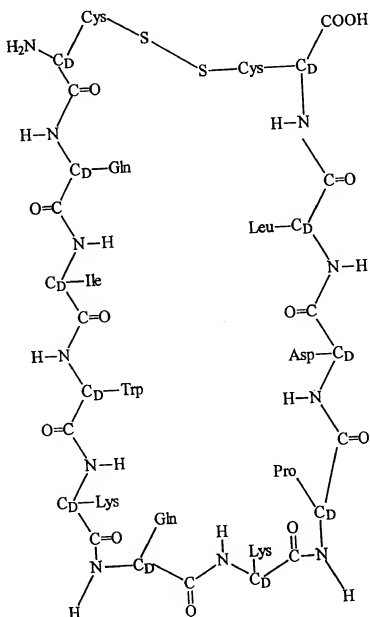
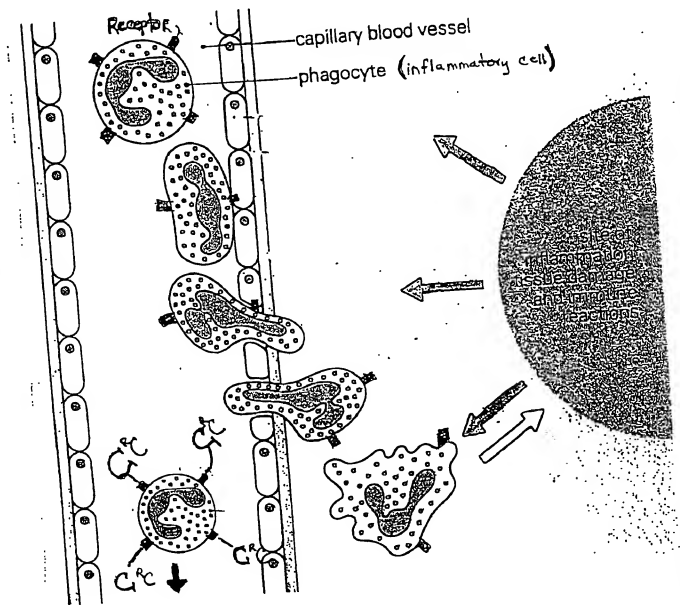


FIGURE 4

00150010-004190



Figures

TARGET FOR VIRAL ENTRY (HIV VIRUS)

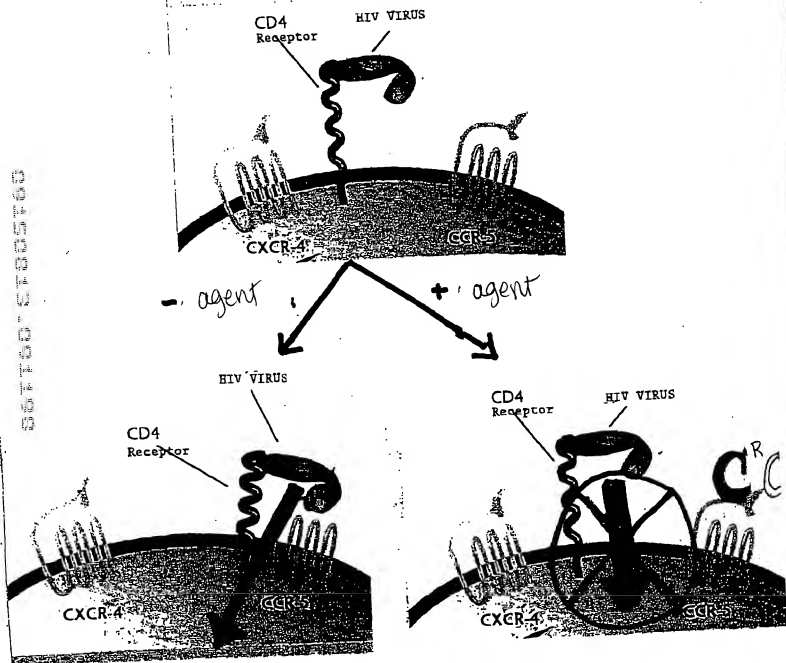
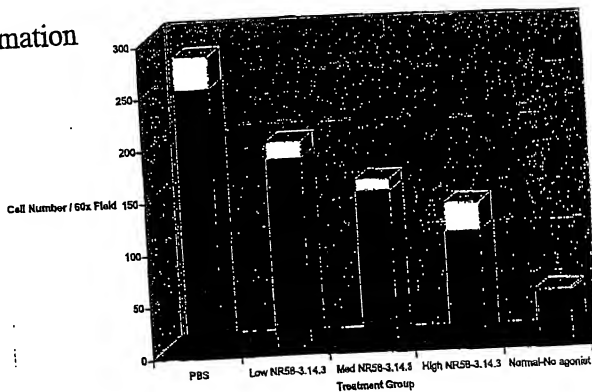


Figure 6

Skin Inflammation Model



Endotoxemia Model

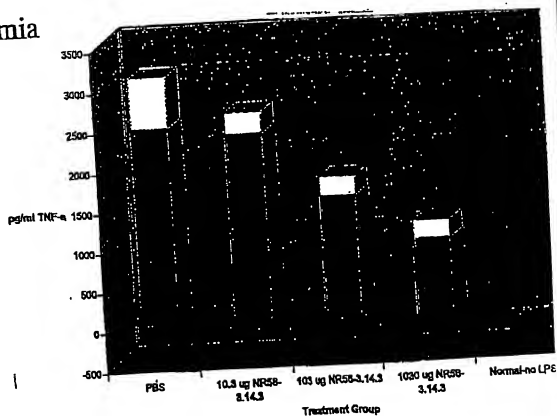


Figure 7

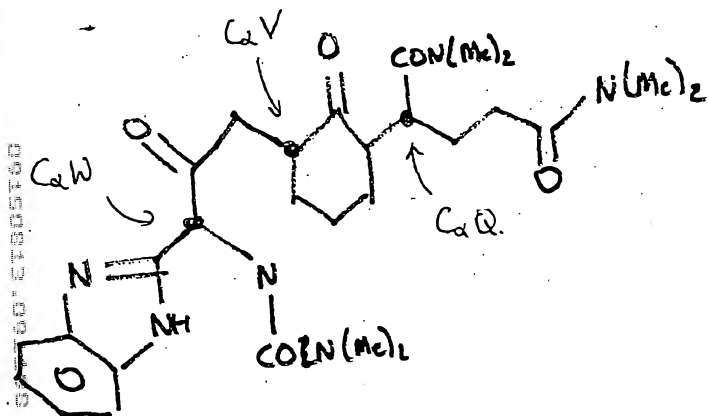


Figure 8

NUMBER OF MACROPHAGES
(Arbitrary units)

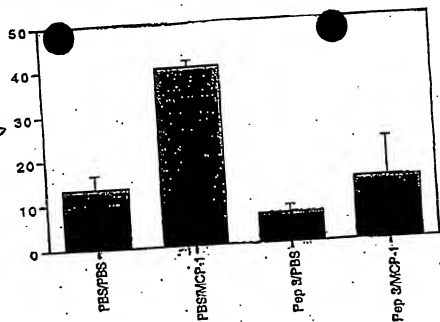


Figure X
9

NUMBER OF B-CELLS

(Arbitrary units)

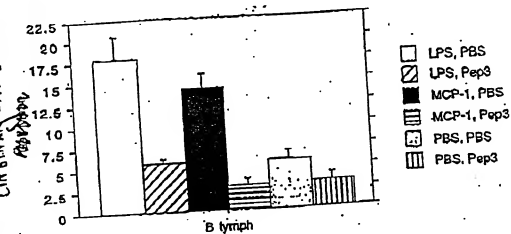


Figure 7₁₀

● THP-1 cells in the presence of HIV

FRACTION
OF
CELLS
INFECTED
(infected/total cells)

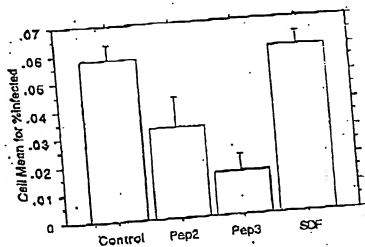


Figure 2

Figure 12

<u>Amino Acid</u>	<u>Codon</u>
Phe	UUU, UUC
Ser	UCU, UCC, UCA, UCG, AGU, AGC
Tyr	UAU, UAC
Cys	UGU, UGC
Leu	UUA, UUG, CUU, CUC, CUA, CUG
Trp	UGG
Pro	CCU, CCC, CCA, CCG
His	CAU, CAC
Arg	CGU, CGC, CGA, CGG, AGA, AGG
Gln	CAA, CAG
Ile	AUU, AUC, AUA
Thr	ACU, ACC, ACA, ACG
Asn	AAU, AAC
Lys	AAA, AAG
Met	AUG
Val	GUU, GUC, GUA, GUG
Ala	GCU, GCC, GCA, GCG
Asp	GAU, GAC
Gly	GGU, GGC, GGA, GGG
Glu	GAA, GAG

FIGURE 13

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala (A)	val; leu; ile	val
Arg (R)	lys; gln; asn	lys
Asn (N)	gln; his; lys; arg	gln
Asp (D)	glu	glu
Cys (C)	ser	ser
Gln (Q)	asn	asn
Glu (E)	asp	asp
Gly (G)	pro	pro
His (H)	asn; gln; lys; arg	arg
Ile (I)	leu; val; met; ala; phe norleucine	leu
Leu (L)	norleucine; ile; val; met; ala; phe	ile
Lys (K)	arg; gln; asn	arg
Met (M)	leu; phe; ile	leu
Phe (F)	leu; val; ile; ala	leu
Pro (P)	gly	gly
Ser (S)	thr	thr
Thr (T)	ser	ser
Trp (W)	tyr	tyr
Tyr (Y)	trp; phe; thr; ser	phe
Val (V)	ile; leu; met; phe; ala; norleucine	leu

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FIGURE 14

Peptide 3

LFL peptide 3(1-12)[MCP-1]: Residues 50-61 of mature hMCP-1
E-I-C-A-D-P-K-Q-K-W-V-Q
L amino acids

LFL peptide 3(3-12)[MCPI] Residues 52-61 of mature hMCP-1
C-A-D-P-K-Q-K-W-V-Q
L amino acids

LFL peptide 3(1-6)[MCP1]: residues 50-55 of mature hMCP-1
E-I-C-A-D-P
L amino acids

LFL peptide 3(7-12)[MCP1]: Residues 56-61 of mature hMCP-1
K-Q-K-W-V-Q
L amino acids

LFL Leu₄peptide3(1-12)[MCP-1]
E-I-C-L-D-P-K-Q-K-W-V-Q
L amino acids

LFL Ser₇peptide3(1-12)[MCP-1]
E-I-C-A-D-P-S-Q-K-W-V-Q
L amino acids

LFL Ile₁₁peptide3(1-12)[MCP-1]
E-I-C-A-D-P-K-Q-K-W-I-Q
L amino acids

LFL Leu₄Ile₁₁peptide3(1-12)[MCP-1]
E-I-C-L-D-P-K-Q-K-W-I-Q
L amino acids

CFL Cys₀Leu₄Ile₁₁Cys₁₃peptide3(1-12)[MCP-1]
C-E-I-C-L-D-P-K-Q-K-W-I-Q-C
L amino acids

LRD Leu₄Ile₁₁ peptide 3(1-12)[MCP-1]
q-i-w-k-q-k-p-d-l-c-i-e
D amino acids

CRD Cys₀Leu₄Ile₁₁Cys₁₃peptide 3(1-12)[MCP-1]
c-q-i-w-k-q-k-p-d-l-c-i-e-c
D amino acids

LFL Ser₇Glu₈Glu₉peptide3(1-12)[MCP1]:Residues 50-61 of mature hMIP1 α
E-I-C-A-D-P-S-E-E-W-V-Q
L amino acids

LFL peptide3(10-12)[MCP-1]
W-V-Q
L amino acids

CFL Cys₀Cys₄ peptide3(10-12)[MCP-1]
C-W-V-Q-C
L amino acids

LRD peptide3(10-12)[MCP-1]
q-v-w
D amino acids

LFL peptide3(7-9)[MCP-1]
K-Q-K
L amino acids

LRD peptide3(7-9)[MCP-1]
k-q-k
D amino acids

LFL peptide 3(7-9)[MIP1 α](MIP1 α specific inhibitor)
S-E-E
L amino acids

LRD peptide3(7-9)[MIP1 α] (MIP1 α specific inhibitor)
c-e-s
D amino acids

LFL peptide3(7-9)[IL-8](IL-8 specific inhibitor)
K-E-N
L amino acids

LRD peptide3(7-9)[IL-8](IL-8 specific inhibitor)
n-e-k
D amino acids

LFL peptide3(7-9)[SDF-1 α](SDF-1 α specific inhibitor)

K-L-K

L amino acids

LRD peptide3(7-9)[SDF1 α] (SDF-1 α specific inhibitor)

k-l-k

D amino acids

LFL Leu₄Ile₁₁Cys₁₃ peptide3(3-12)[MCP-1]

L-D-P-K-Q-K-W-I-Q-C

L amino acids

CRD Leu₄Ile₁₁Cys₁₃ peptide3(3-12)[MCP-1]

c-q-i-w-k-q-k-p-d-l-c

D amino acids

³H-Ala CRD-Leu₄Ile₁₁Cys₁₃ peptide 3(3-12)[MCP-1](D-Ala attached to Asp residue of CRD-Leu₄Ile₁₁Cys₁₃ peptide 3(3-12)[MCP-1])

³H-L-Leu LRD Cys₁₃ peptide3(3-12)[MCP-1]

c-q-i-w-k-q-k-p-d-L-c

D and L amino acids

LFL SES

S-E-S

L amino acids

LFL KKK

K-K-K

L amino acids

LFL Cys₄ peptide3(10-12)[MCP-1]

W-V-Q-C

L amino acids

LRD Cys₄ peptide3(10-12)[MCP-1]

c-q-v-w

D amino acids

LFL Ile₁₁Cys₁₃peptide3(10-12)[MCP-1]

W-I-Q-C

L amino acids

LRD Cys₁₃Ile₁₁peptide3(10-12)[MCP-1]

cqiw

D amino acids

LRD peptide3(7-12)[MCP-1]

q-v-w-k-q-k

D amino acids

CFL Cys₀Cys₁₃peptide3(7-12)[MCP-1]

C-K-Q-K-W-V-Q-C

L amino acids

CRD Cys₀Cys₁₃peptide3(7-12)[MCP-1]

c-q-v-w-k-q-k-c

D amino acids

LFL peptide3(10-12)[RANTES]

WVR

L amino acids

LRD peptide3(10-12)[RANTES]

rvw

D amino acids

LFL peptide3(10-12)[SDF-1]

W-I-Q

L amino acids

Peptide 2

LFL peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1

S-Y-R-R-I-T-S-S-K-C-P-K-E-A-V

L amino acids

CFL Cys₀Cys₁₆peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1

C-S-Y-R-R-I-T-S-S-K-C-P-K-E-A-V-C

L amino acids

LRD peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1

v-a-e-k-p-c-k-s-s-t-i-r-r-y-s

D amino acids

CRD Cys₀Cys₁₆peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1
c-v-a-e-k-p-c-k-s-t-i-r-y-s-c
D amino acids

LFL peptide 2(1-15)[SDF1]: Residues 26-40 of mature hSDF-1 β
H-L-K-I-L-N-T-P-N-C-A-L-Q-I-V
L amino acids

CFL Cys₀Cys₁₆peptide 2(1-15)[SDF1]: Residues 26-40 of mature hSDF-1 β
C-H-L-K-I-L-N-T-P-N-C-A-L-Q-I-V-C
L amino acids

LRD peptide 2(1-15)[SDF1]: Residues 26-40 of mature hSDF-1 β
v-i-q-l-a-c-n-p-t-n-l-i-k-l-h
D amino acids

CRD Cys₀Cys₁₆peptide 2(1-15)[SDF1]: Residues 26-40 of mature hSDF-1 β
c-v-i-q-l-a-c-n-p-t-n-l-i-k-l-h-c
D amino acids

LFL peptide 2(1-14)[MIP-1 α]: Residues 28-41 of hMIP-1 α
D-Y-F-E-T-S-S-Q-C-S-K-P-G-V
L amino acids

LRD peptide 2(1-14)[MIP1 α]: Residues 28-41 of mature hMIP1 α
v-g-p-k-s-c-q-s-t-e-f-y-d
D amino acids

LFL peptide 2(1-16)[IL8]: Residues 27-42 of mature hIL8
E-L-R-V-I-E-S-G-P-H-C-A-N-T-E-I
L amino acids

LFL Peptide 2(1-10)[MCP-1]: Residues 28-37 of hMCP-1
S-Y-R-R-I-T-S-S-K-C
L amino acids

LFL peptide 2(10-15)[MCP-1]: Residues 37-42 of hMCP-1
C-P-K-E-A-V
L amino acids

LFL peptide 2(1-5)[MCP-1]: Residues 28-32 of hMCP-1
S-Y-R-R-I
L amino acids

LFL peptide 2(6-10)[MCP-1]: Residues 33-37 of hMCP-1
T-S-S-K-C
L amino acids

LFL peptide 2(1-9)[MIP-1 α]: Residues 28-36 of hMIP-1 α
D-Y-F-E-T-S-S-Q-C
L amino acids

LFL peptide 2(9-14)[MIP-1 α]: Residues 36-41 of hMIP-1 α
C-S-K-P-G-V
L amino acid

LFL Cys₀Ser₁₀Cys₁₆peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1
C-S-Y-R-R-I-T-S-S-K-S-P-K-E-A-V-C
L amino acids

CFL Cys₀Ser₁₀Cys₁₆peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1
C-S-Y-R-R-I-T-S-S-K-S-P-K-E-A-V-C
L amino acids

LRD Cys₀Ser₁₀Cys₁₆peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1
c-v-a-e-k-p-s-k-s-s-t-i-r-r-y-s-c
D amino acids

CRD Cys₀Ser₁₀Cys₁₆peptide 2(1-15)[MCP-1]: Residues 28-42 of hMCP-1
c-v-a-e-k-p-s-k-s-s-t-i-r-r-y-s-c
D amino acids

S01180-21003150

Sequence	DARC Binding	THP-1 Migration		
		MCP-1	MIP-1 α	SDP-1 α
SYRRTSSKCPKEAV	350 nM	ns	ns	ns
vaekpckstirrys	18 μ M	ns	ns	ns
SYRRTSSK	22 μ M	ns	ns	ns
SYRRI	>100 μ M	ns	ns	ns
TSSKC	>100 μ M	ns	ns	ns
CPKEAV	>100 μ M	ns	ns	ns
HLKILNTNCALQIV	19 μ M	10 μ M	40 μ M	7 μ M
DYFETSSQCSKPGV	>100 μ M	ns	ns	ns
vqpkscqsstefyd	>100 μ M	ns	ns	ns
DYFETSSQC	>100 μ M	ns	ns	ns
CSKPGV	>100 μ M	ns	ns	ns

Figure 15

Sequence	Mol Wt.		Duffy Binding ED-50	MCP-1 ED-50	MIP-1α ED-50	RANTES ED-50	SDF-1α ED-50	IL-8 ED-50	Other Data
AQPDAINAPVTCC	1302		90nM	ns	ns	-	ns	ns	
SVRRTSSKCPKEAV	1725		100nM	ns	ns	-	ns	-	
veekpckastictys	1725		18μM	ns	ns	-	ns	-	
HKTLTNPCLQIV	1677.3		19μM	10μM	40μM	-	7μM	-	
DYFETSSQCKPGV	1549		>100μM	ns	ns	-	ns	-	
vppkscqgsteftyd	1549		>100μM	ns	ns	-	ns	-	
SVRRTSSKNC	1097.4		22μM	ns	ns	-	ns	-	
CPKEAV	645.8		>100μM	ns	ns	-	ns	-	
SVRRJ	693.9		>100μM	ns	ns	-	ns	-	
TSKNC	525.7		>100μM	ns	ns	-	ns	-	
DYFETSSQCK	1079.2		>100μM	ns	ns	-	ns	-	
CSKPGV	589.8		>100μM	ns	ns	-	ns	-	

Figure 16

867160-27005160

ETCADDPKQKWQ	1445		6μM	8μM	7.5μM		13.5μM	10μM	
CADFSQKWQ	1202		-	8μM	6.5μM		9μM	8.5μM	
ccvkkkqdaac	1305		3μM	100nM	-		-	-	
ccvkkkqdaac	1305		40μM	30nM	-		-	-	
ETCADDP	647		-	25μM	20μM		18.5μM	16μM	
KQKWQ	816		15μM	7μM	5μM		5.5μM	5μM	
ETCADDPKQKWQ	1487		-	8μM	7μM		2.5μM	3μM	
ETCADDPKQKWQ	1404		25μM	7μM	5.5μM		4μM	3μM	
ETCADDPKQKWQ	1459		-	5.5μM	3.5μM		7μM	2μM	
ETCADDPKQKWQ	1501		90μM	2μM	2μM		4μM	3.5μM	
WQ	431.5		1μM	8μM	7.5μM		1.5μM	2.25μM	1μM
KQK	464.5		50μM	7μM	>100μM		>100μM	>100μM	>100μM
SRR	399.4		>100μM	>100μM	>100μM		>100μM	>100μM	>100μM
KEN	425.4		>100μM	>100μM	>100μM		>100μM	>100μM	

037780-CT805100

KLK	516.6		>100µM	>100µM	>100µM	>100µM	>100µM	>100µM
cqlukgkpdle	1359		>100µM	1nM		350nM	10nM	Note 1
cqlukgkpdle	1448			>100µM				Note 2
cqlukgkpdle	1472.2			10nM				
SES	357.3		>100µM	>100µM				
KLK	609.8		>100µM					

Note 1: *In Vivo* effect- Abolishes macrophages in an *in vivo* rat intradermal study induced by 500µg MCP-1. 300µg IV and 10 mg SQ 30 minutes prior to MCP-1.
 Note 2: *In vivo* effect- Abolishes macrophages in an *in vivo* rat intradermal study induced by 500µg MCP-1. 300µg IV and 10 mg SQ 30 minutes prior to MCP-1.
 Date (cc) is attached to the base (cc)

Note 2: in same study as Note 1 above, no effect on macrophages seen.

Study Design Table

Group	Animal #	N	RX	RX dose/route T=30 min	Dermal Agonist	Dermal Agonist Dose (ng in 50 ul) T=0	Hour of Sacrifice
1	1,2,3	3	PBS	200 ul: iv 200 ul: SQ back	PBS LPS MCP-1 MCP-1	0 50 100 500	20-24
2	4,5,6	3	NR58-3.14.3	3 ug: iv 100 ug: SQ back	PBS LPS MCP-1 MCP-1	0 50 100 500	20-24
3	7,8,9	3	NR58-3.14.3	30 ug: iv 1 mg: SQ back	PBS LPS MCP-1 MCP-1	0 50 100 500	20-24
4	10,11,12	3	NR58-3.14.3	300 ug: iv 10 mg: SQ back	PBS LPS MCP-1 MCP-1	0 50 100 500	20-24

Figure 17